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Abstract

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Project Title:	High Throughput Screen for Inhibitors of the HIV Rev-RRE RNA Interaction

Abstract: *DESCRIPTION (provided by applicant):* This proposal outlines a plan to carry out a high throughput screen (HTS) for inhibitors that block formation of the HIV Rev-Rev Response Element (RRE) RNA complex, at one of the MLSCN Centers. Rev is an RNA binding protein that is critical in regulating the shift from early to late patterns of viral gene expression, and it is specifically implicated in facilitating nuclear transport of viral mRNAs into the cytoplasm. The RRE is an RNA secondary structure element in the HIV mRNA that is the binding site for the Rev protein. This represents a novel target for inhibition of HIV for which there are no therapeutics. A validated HTS for Rev-RRE inhibitors has been developed using a FRET assay to monitor binding of a synthetic peptide and a synthetic RNA that have been labeled with fluorescent groups. Statistical analysis of control plates that validate the assay are presented, as well as the results from a pilot scale screen of ~24,000 compounds. A plan for follow-up screens for the primary hits from the MLSCN screen is presented. In addition, cell-based assays for inhibition of the Rev-RRE interaction are described. Finally, the use of Rev-RRE inhibitors to further our biochemical, biophysical, and cellular understanding of Rev function is outlined.

Thesaurus Terms: high throughput screen, HTS, HIV Rev-Rev Response Element, RRE, Molecular Libraries Screening Centers Network, MLSCN, RNA binding protein, viral mRNA, FRET assay, synthetic peptide, Rev-RRE interaction

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